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RANKING OF LIKELIHOOD OF RE-EMERGENCE OF SELECTED VECTORBORNE DISEASES IN IRELAND

Report by the Vectorborne Disease Sub-Committee
of the
HPSC Scientific Advisory Committee

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1. Introduction

Over the last number of years, Southern and Eastern Europe has been the setting for the emergence (or re-emergence)[1] of a range of vectorborne diseases that would have, until recently, been considered to be exotics. Mosquito-borne diseases, including malaria, dengue, West Nile Virus (WNV) and chikungunya fever (CHIK), frequently cause outbreaks/epidemics in tropical and sub-tropical parts of the world. More recently, the spread of WNV into the United States (US), chikungunya into Italy, *Plasmodium vivax* malaria in Greece and dengue into Madeira have given rise to concerns that temperate parts of Europe could be at risk from mosquito-borne disease. [1,2,3,4]

Similarly, while the tick-borne disease Crimean-Congo haemorrhagic fever (CCHF) has been endemic in parts of the Balkans, the first European reports of human infections were only made in the last decade, from Turkey and Greece.[1,2]

One example of vectorborne disease emergence in the veterinary field is the discovery of *Schmallenberg* virus, a *Culicoides*-transmitted teratogenic orthobunyavirus affecting ruminants, which is not believed to pose a risk to humans.[1] First identified in central Europe in November 2011, it had reached Ireland by October 2012.[2]

Another example of vectorborne disease emergence in the veterinary field is blue tongue virus, a *Culicoides* (midge) borne disease affecting cattle and sheep, which until 2006 was reported only in southern regions of the EU including parts of Italy, Spain, France and Portugal. In August 2006, the first ever Northern European outbreaks were reported in The Netherlands, Belgium, Germany and France. Further outbreaks were reported in 2007 and 2008, including in the United Kingdom and Sweden.[3]

In response to concern about emergence and re-emergence in Europe of several vectorborne diseases, the European Centre for Disease Prevention and Control (ECDC) has devised a strategy for their Emerging and Vectorborne Diseases Programme which includes diseases transmitted by mosquitoes, ticks and sand-flies. Many high quality publications and documents have been and continue to be produced by ECDC, including many Rapid Risk Assessments. This report draws heavily on several of these. These initiatives are taking place in the wider context of similar work undertaken by the European Food Safety Authority (EFSA) in respect of such diseases and horizon scanning in animals. (http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/emerging_and_vector_borne_diseases/Pages/index.aspx)

[1] The term "emergence" will be used throughout this document and refers both to emergence of diseases not before seen in Ireland or the re-emergence of disease previously established in Ireland.

The ECDC strategic priorities for emerging and vectorborne diseases are outlined in Box 1.

Box 1. ECDC strategic priorities [4]

To improve the preparedness and response towards emerging vectorborne diseases, the Emerging and Vectorborne Diseases Programme develops its activities along the following strategic areas:

1. To improve the knowledge and develop a strategy for future activities in the field of vector and vectorborne diseases surveillance in order to strengthen preparedness in the EU for these, especially on tick-borne diseases (Lyme borreliosis, tick-borne encephalitis, rickettsioses and Q-fever*) and mosquito-borne diseases (West Nile fever, malaria, dengue and chikungunya).

2. To encourage the exchange of scientific and public health expertise in the field of EVD.

3. To contribute to the early response to emerging threats by linking with the scientific expertise and diagnostic laboratory capacity in Europe and provide support to outbreak assistance teams in terms of diagnostic capacity, scientific advice and surveillance tools.

4. To increase public and health professionals' awareness of vectorborne diseases.

* While Q fever is listed in the ECDC strategic priorities for Emerging and Vectorborne Diseases, it is not included in this assessment as the disease is believed not to be primarily transmitted by vectors

Any factors that facilitate the introduction and establishment of disease vectors, reservoir hosts or pathogens in new geographic areas could lead to the emergence of a disease. These factors include international travel and trade, e.g. legal and illegal trade in animals and animal products, new agricultural practices and land-use patterns, socio-demographic evolution and climatic changes.

This document attempts to evaluate the likelihood of an indigenous threat to Ireland from vectorborne transmission of human disease. An algorithm devised by Marieta Braks (RIVM & Vbornet)[5] was used to assess the threat/risk level posed by the selected vectorborne diseases, in order that the diseases could be ranked/prioritised in terms of their likely emergence through vectorborne transmission in Ireland. Another useful outcome of this exercise is the identification of knowledge gaps.

This is the first attempt in Ireland to undertake a risk assessment for the potential emergence of indigenous vectorborne disease. The method used here simply ranks the risk of emergence without taking into account the public health significance of the introduction of the selected diseases. In formulating recommendations on foot of this information other factors need to be taken into consideration, including disease severity (both for the general population and for high-risk groups).

This report does not assess the threat to Irish residents during travel abroad. In addition, the threat to the Irish blood supply from returning travellers is beyond the scope of this exercise.

2. Material and methods

2.1 Diseases included in the report

Selection of diseases for this review was based upon the existence or otherwise of documented evidence of transmission by a vector in Europe within the last two decades.[6,7,8,9]

Malaria, WNV, dengue, chikungunya, Sindbis and Usutu viruses were evaluated among the mosquito-borne diseases. Among the tick-borne diseases, Lyme borreliosis, Congo Crimean Haemorrhagic Fever (CCHF), louping-ill, tick-borne encephalitis (TBE), tularaemia and babesiosis were selected for inclusion. Leishmaniasis and sandfly viruses were selected among the diseases transmitted by Phlebotomines.

Examples of diseases excluded from the assessment include: Q fever (zoonotic transmission is the most significant transmission route); Chagas (while vectorborne in Latin America, the main concern in Europe centres on its potential for transfusional, congenital and laboratory-accident transmission)[10]; and tick-borne relapsing fevers (not a significant pathogen in Europe).

A brief description of the clinical features, known distribution, likely vectors and reservoirs for each of the selected diseases is given in Appendix A.

2.2 Threat assessment methodology

Table 1 illustrates the disease likelihood rank assessment tool which was used to assess the likelihood rank of the selected vectorborne diseases. In the absence of indigenous disease, the presence of the vector in Ireland and the existence of a source of the pathogen, are used to assess how likely the possibility of threat of the human disease is. Diseases which receive a high likelihood rank (4-5) being considered the least likely to become established and pose a risk to human health. Diseases move up the threat level from where the vector is not present, to vector being present but there is no known pathogen reservoir in the country, to being endemic.

Table 1: Vectorborne disease likelihood rank assessment tool [5]

Indigenous cases (Y/N)	Pathogen present (imported cases/present in animal reservoir/present in vector population) (Y/N)	Vector present (Y/N)	Likelihood Rank
Y	**Y**	**Y**	Likelihood rank 1
N	**Y**	**Y**	Likelihood rank 2
N	N	**Y**	Likelihood rank 3
N	**Y**	N	Likelihood rank 4
N	N	N	Likelihood rank 5

Essentially the following decision tree was applied to each of the selected diseases (Figure 1).

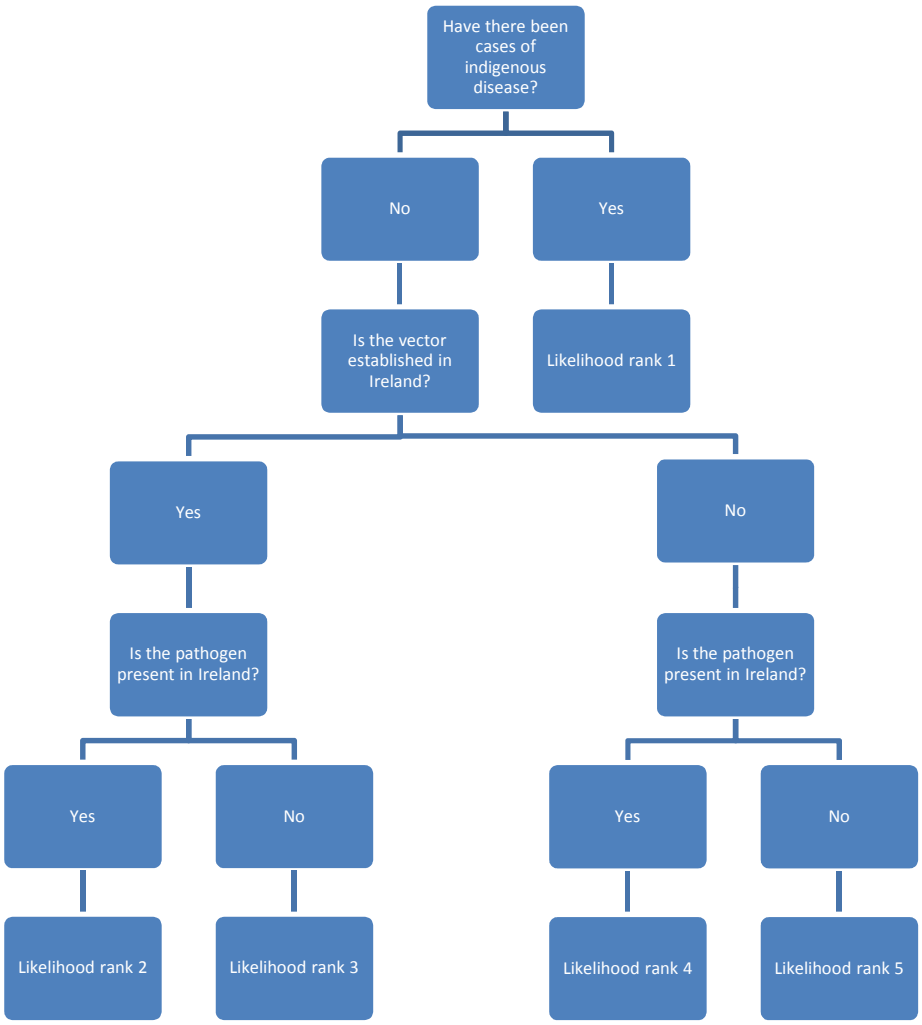

Figure 1: Decision tree for assessing disease likelihood rank

2.3 Data sources

2.3.1 Disease distribution

The occurrence of indigenous disease was assessed using data from several sources:

(i) Irish notifiable disease data provided by HPSC from the national notifiable infectious disease database, CIDR (Computerised Infectious Disease Reporting system)

(ii) laboratory data on selected non-notifiable virus diseases obtained from the National Virus Reference Laboratory (NVRL)

(iii) published literature

(iv) conference proceedings

(v) personal communication from clinicians working in the field of infectious disease in Irish hospitals.

2.3.2 Vector occurrence in Ireland

The presence of the vectors in Ireland was assessed based on available surveillance information from published literature on surveys in Ireland, from international reports showing the known distribution of vectors and in one instance from unpublished information from an ongoing study.

For vectors where insufficient data were available, an assessment was made by members of the sub-committee on whether they were likely or unlikely to be present in Ireland based on factors such as climate and present known distribution.

2.3.3 Pathogen reservoir in Ireland

Assessment of the presence of a potential reservoir of the pathogen in Ireland was accomplished in different ways depending on the pathogen.

- For diseases for which humans can serve as the reservoir, the occurrence of indigenous or imported cases of human disease was sufficient to give a positive response to this question. For these diseases, the same human disease information sources listed above were used to establish the occurrence of imported disease.

- For diseases where a vector is present in Ireland, detection of the pathogen in the vector could be used.

- Similarly, for diseases for which the reservoir host was an animal host, the detection of the pathogen in an animal reservoir would provide evidence of presence.

For diseases where insufficient data were available, as assessment was made by members of the sub-committee of whether they were likely or unlikely to be present in Ireland.

3. Results

3.1 Indigenous disease occurrence in Ireland

The known occurrence of indigenous and travel-associated vectorborne disease in Ireland is outlined in table 2. Where indigenous cases have been reported, these data were also used to complete Table 5.

3.1.1 Mosquito-borne diseases

Malaria is a statutorily notifiable disease in Ireland as defined by the Infectious Disease Regulations 1981 (SI No. 390 of 1981). Between 70 and 90 notifications are reported annually, all associated with travel to malarious areas in Africa, Asia and South America.[11,12] There have also been reports of imported human cases of dengue, chikungunya and WNV. However, no indigenous cases have been reported.[13,14]

For Usutu and Sindbis viruses, we are not aware of any case reports, and it seems unlikely they are currently present in Ireland.

Table 2: Reported diagnoses of human disease (indigenous and imported) in Ireland

	Imported cases	Indigenous cases	Data source
Mosquito-borne diseases			
Chikungunya	Y	N	14, 27
Dengue	Y	N	14, 27
Malaria	Y	N	11,12, 27
Sindbis	Unknown	Unknown but unlikely	Opinion of the committee
Usutu	Unknown	Unknown but unlikely	Opinion of the committee
West Nile fever (WNV)	Y	N	13,14, 27
Tick-borne diseases			
Babesiosis	Unknown	Y	6, 15, 28, 29,
CCHF	N	N	27
Louping-Ill	Unknown	Unknown but possible	Opinion of the committee
Lyme borreliosis	Y	Y	22-26, 27
Tick-borne encephalitis	N	N	27
Tularaemia	N	N	27
Sandfly-borne diseases			
Leishmaniasis	Y	Unknown but unlikely	Sam McConkey, Consultant in Infectious Diseases, Beaumont Hospital personal communication
Sandfly fever viruses (sandfly fever Sicilian virus, sandfly fever Naples virus, and Toscana virus)	Unknown but plausible	Unknown but unlikely	Opinion of the committee

3.1.2 Tick-borne diseases

Lyme borreliosis is known to be endemic in the human population in Ireland.[16,17,18,19,20] In 2007, 71 specimens referred from Irish hospital laboratories to the HPA's Lyme Borreliosis Unit in Southampton were confirmed positive for Lyme borreliosis. This suggests a crude incidence rate of 1.67 per 100,000 for Lyme borreliosis in Ireland that year (Dr Sue O Connell (Public Health England) and Dr Robert Smith (Public Health Wales) personal communication). However, a recent study in the west of Ireland reported by Moloney & colleagues at Galway University Hospital suggests that the disease incidence may be higher in the Galway area.[22]

Lyme neuroborreliosis was made a notifiable disease in January 2012 in Ireland. In 2014, 18 cases of neuroborreliosis were notified to HPSC.[27]

Although both CCHF and tularaemia are notifiable diseases, no cases have been notified in Ireland (either indigenous or foreign-travel associated).[21] TBE became notifiable in September 2012 under the disease viral encephalitis. Since NVRL commenced testing service for TBE in 2009, no cases have been diagnosed (J Connell NVRL, personal communication and CIDR).

From case studies in published literature, babesiosis in humans has been described in Ireland, but only in asplenic patients.[22,23] Louping-ill has been described in sheep in Ireland, however we are not aware of any confirmed occurrences of human cases.[24]

3.1.3 Sandfly-borne diseases

While there are no official data sources on the incidence of leishmaniasis in Ireland, imported cases of disease have been diagnosed here (Sam MacConkey, personal communication). Imported disease has also been reported in dogs (Donal Sammin, DAFM personal communication). For sandfly fevers, we are unaware of any case reports, although it seems plausible that from time-to-time imported cases of these diseases do occur.

3.2 Vector presence in Ireland

Table 3 below lists the vectors implicated in transmission of the selected diseases in Europe, and their occurrence in Ireland.

3.2.1 Mosquitoes

There have been reports of *Culex pipiens*, from both published literature[25,26,32] and also from Environmental Health invasive mosquito surveillance (Tom Kelly and Mary Keane -personal communication). *C. pipiens* is primarily an ornithophilic species, which can serve as a vector of WNV, Sindbis virus and Usutu virus in humans. There have also been reports of *Anopheles algeriensis* Theobald, *Anopheles clavigar* (Meigen*), Anopheles maculipennis* complex (including *Anopheles messeae* Falleroni) and *Anopheles plumbens* Stephens in Ireland [25,32]. However, there have been no reports of *Ae. aegypti or Ae. albopictus,* which would be required for transmission of Chikungunya or dengue.

3.2.2 Ticks

The most important human disease vector present in Ireland is *Ixodes ricinus.*[27,28,29,30,31] This tick serves as a vector for Lyme borreliosis. It can also serve as a vector for louping-ill, tick-borne relapsing fevers, and tularaemia, among others. Currently available maps of tick distribution published by ECDC indicate that species such as *Haemaphysalis, Hyalomma* and *Dermacentor* are unlikely to occur in Ireland.[32,33,28]

3.2.3 Sandflies

Currently available maps of sandfly distribution published by ECDC indicate that phlebotomimes are unlikely to occur in Ireland.[34]
(http://ecdc.europa.eu/en/activities/diseaseprogrammes/emerging_and_vector_borne_diseases/Pages/VBORNET_maps_sandflies.aspx).

Table 3: Disease vectors and their occurrence in Ireland

Disease	Vector	Vector occurrence in Ireland (Y/N)	Information source	For vectors not currently present in Ireland, is there potential for establishment based on current climate?
Mosquito-borne diseases				
Chikungunya fever	*Aedes* mosquitoes (*A. aegypti, A. albopictus* and *A. polynesiensis*).	Not reported	25 & T Kelly, M Keane, (personal comm.)	Not currently
Dengue	*Aedes* mosquitoes (mainly *A. aegypti, A. albopictus*)	Not reported	25 & T Kelly, M Keane, (personal comm.)	Not currently
Malaria	*Anopheles* species, about 20/430 species are important in transmission	Some species present in Ireland; *An. algeriensis* Theobald, *An. clavigar* (Meigen), *An. maculipennis* complex and *An. plumbens* Stephens	25 & T Kelly, M Keane, (personal comm.)	NA
Sindbis virus	*Culex*, *Culiseta* and to a lesser extent *Aedes* mosquitos	Y	25 & T Kelly, M Keane, (personal comm.)	NA
Usutu virus	*Culex pipiens*	Y	25 & T Kelly, M Keane, (personal comm.)	NA
West Nile Virus	*Cx. pipiens*, Cx modestus	Y, *Cx pipiens*, N, *Cx. modestus*	25 & T Kelly, M Keane, (personal comm.)	NA
Tick-borne diseases				
Babesiosis	*Ixodes, Dermacentor, Rhipicephalus, Haemaphysalis etc*	Yes, *I. ricinus* Unlikely for others	27, 32, 33,	NA
Crimean-Congo Haemorrhagic Fever	*Hyalomma marginatum*	Unlikely	28, 32, 33	
Louping-Ill	*Ixodes ricinus*	Y	33, 28, 32	NA
Lyme borreliosis	*Ixodes ricinus , I. uriae*	Y	27, 34, 32	NA
Tick-borne encephalitis	*Ixodes ricinus, I. persulcatus*	Y, *I. ricinus*	28, 32	NA
Tularaemia	*Dermacentor reticulatus, D. marginatus*, *Ixodes ricinus*, and *Haemaphysalis concinna* ticks	Yes, *I. ricinus* Unlikely, *Dermacentor,* Unlikely, *H. concinna*	28, 30, 32, 33	NA
Sandfly-borne diseases				
Leishmaniasis	*Phlebotomus ariasi*, *P. perniciosus* and *P. perfiliew* for *L. infantum* *P. sergenti sensu lato* for *L. tropica*	Unlikely	34, 40	No
Sandfly fever viruses (sandfly fever Sicilian virus, sandfly fever Naples virus, and Toscana virus)	*P. papatasi, P. perniciosus, P. perfiliewi, P. neglectus* and *P. papata*	Unlikely	34, 40	No

NA = not applicable –at least one possible vector already present in Ireland

Table 4: Potential presence of pathogen in Ireland

Disease	Information sources	Pathogen present in human (imported) cases[†]	Pathogen present in animal reservoir[‡]	Pathogen present in vector population[§]	Pathogen present in Ireland (Y/N)[**]
Mosquito-borne diseases					
Chikungunya fever	14, 27	Y	NA	NA	**Y**
Dengue	14, 27	Y	NA	NA	**Y**
Malaria	11, 12, 27	Y	NA	Unknown but unlikely	**Y**
Sindbis virus		NA	Unknown but unlikely	Unknown but unlikely	Unlikely
Usutu virus		NA	Unknown but unlikely	Unknown but unlikely	Unlikely
West Nile Virus	35, 27	NA	N	Unknown but unlikely	Unlikely
Tick-borne diseases					
Babesia	36, 37, 38		Y		**Y**
Crimean-Congo Haemorrhagic Fever		N	Unknown but unlikely	NA	Unlikely
Louping-Ill		NA	Y	Yes by inference	**Y**
Lyme borreliosis	22-27	NA	Yes by inference	Y	**Y**
Tick-borne encephalitis	27	NA	Unknown but unlikely	Unknown but unlikely	Unlikely
Tularaemia		NA	Unknown but unlikely	Unknown but unlikely	Unlikely
Sandfly-borne diseases					
Leishmaniasis		NA	Unknown	NA	Unlikely
Sandfly fever viruses (sandfly fever Sicilian virus, sandfly fever Naples virus, and Toscana virus)		NA	NA	NA	Unlikely

[†] NA if humans cannot serve as reservoir hosts
[‡] NA if no animal reservoir host or if animal reservoir host not present in Ireland
[§] NA if vector not present in Ireland
[**] Inference from three previous columns (Yes if any of three previous columns =Yes)

3.3 Potential presence of pathogen in Ireland

For the criterion "Pathogen presence in Ireland" to be met, the pathogen must have been detected at some time either in a reservoir host or in a vector population in Ireland. In some instances, humans serve as the reservoir host. For example, imported cases of dengue, chikungunya, malaria and WNV have been described.[11,12, 14] Imported cases of the first three diseases could potentially serve as disease reservoirs were they to be imported into Ireland, and therefore the criterion is recorded as being met. It should be noted that cases of dengue and chikungunya should be viraemic when they arrive in Ireland for the pathogen to be present. For WNV, humans are dead-end hosts and cannot serve as a host reservoir. In this instance, evaluation of this criterion is through passive surveillance of known animal reservoirs by Department of Agriculture, Food and the Marine (DAFM).[41] Evidence for the occurrence of Babesia and louping-ill virus in animal reservoirs was taken from published literature.

Table 4 lists the available data on pathogen presence in Ireland in reservoir hosts or vectors. The final column in the table summarises the data from the first three columns and is used in the "pathogen present" element of the likelihood rank assessment in table 5.

3.4 Likelihood ranks

Table 5 summarises the information assembled on the three criteria and the threat likelihood ranks established for each of the selected diseases.

Within the mosquito-borne diseases, the disease with the highest rank for threat was malaria, followed by WNV, Sindbis and Usutu.

Of all the diseases evaluated, the only subgroup among which there was current vectorborne disease transmission were tick-borne diseases. Among these, Lyme borreliosis ranked highest in likelihood rank alongside babesiosis, with louping-ill following in likelihood rank 2.

Both sandfly-borne diseases ranked very low due to the absence of sandfly vectors in Ireland.

Table 5: Ranking of diseases based on threat/risk assessment methodology

Disease	Indigenous cases (Y/N)	Pathogen present (Y/N)	Vector present (Y/N)	Likelihood rank
Mosquito-borne diseases				
Chikungunya fever	N	Y[††]	N	**4**
Dengue	N	Y[‡‡]	N	**4**
Malaria	N	Y	Y	**2**
Sindbis virus	Unlikely	Unlikely	Y	**3**
Usutu virus	Unlikely	Unlikely	Y	**3**
West Nile Virus	N	Unlikely	Y	**3**
Tick-borne diseases				
Babesiosis	Y	Y	Y	**1**
Crimean-Congo Haemorrhagic Fever	N	Unlikely	Unlikely	**5**
Louping-Ill	Unlikely	Y	Y	**2**
Lyme borreliosis	Y	Y	Y	**1**
Tick-borne encephalitis	N	Unlikely	Y	**3**
Tularaemia	N	Unlikely	Y	**3**
Sandfly-borne diseases				
Leishmaniasis	Unlikely	Unlikely	Unlikely	**5**
Sandfly fever viruses (sandfly fever Sicilian virus, sandfly fever Naples virus, and Toscana virus)	Unlikely	Unlikely	Unlikely	**5**

4. Drivers of Vectorborne Disease Emergence

Disease transmission and emergence is driven by a range of factors including socio-economic development, urbanisation, land use, migration and globalisation[39]. Many of the examples of vectorborne disease (re-)emergence in the European Union in recent years were facilitated by virus introduction into areas which had habitats that were already vector competent, e.g. malaria in Greece, chikungunya in Italy, dengue in Madeira, and on the veterinary side, Schmallenberg virus and blue tongue in Northern Europe. Globalisation and trade was also a driver of vector spread in the distribution of *Ae. albopictus* through southern Europe over the last decade. In areas that do not already have climatic conditions suitable for a competent vector population, a further potential driver of disease emergence is climate change, making this an important facet in the assessment of potential disease threats.

[††] would need to be viraemic
[‡‡] would need to be viraemic

4.1 Globalisation –trade, travel and migration

The Central Statistics Office (CSO) have reported that in 2012, over six million overseas trips were taken by Irish residents, and that in the same time period, around six and half million trips were made by visitors to Ireland.[40] And according to CSO Census 2011, more than half a million Irish residents were described as non-nationals (12% of the population), with a particularly high increase in the number of people from Central and Eastern Europe in the last nine years.[41] It is also likely that non-Irish living in Ireland have different travel patterns than Irish residents when taking overseas trips. These changes illustrate the potential for introduction of imported cases of diseases not currently endemic in Ireland, and the need for awareness by clinicians of the diversity of differential diagnoses for illnesses that may be travel related. Trade in used tyres and lucky bamboo was cited as contributing to the introduction of *Ae. albopictus* in Southern Europe and The Netherlands respectively. There is potential too for introduction of vector species into Ireland in cargo travelling through air and seaports.

4.2 Climate Change

Weather patterns and climate can both influence transmission cycles and the human incidence of vectorborne disease, through their effects on disease reservoirs, vector populations and activity, and human interaction with the environment. A review by Semenza and Menne looked at the available evidence for the role of climate in disease incidence, and research that has been undertaken into predicting the effect of climate change on vectorborne disease in Europe.[42]

Among the mosquito-borne illnesses, a climate model for WNF suggests a higher risk associated with mild winters, dry springs and summers and wet autumns. High rainfall and sunshine were linked to the aggressiveness of *C. modestus* during a WNF outbreak in Southern France. The 1996-7 outbreak in Romania and the 2000 outbreak in Israel both coincided with heatwaves. Dry weather was also associated with higher reproduction of *C. pipiens* and concentration of vectors with their avian hosts. Temperature is also a factor in dengue transmission, with increases in temperature predicted to increase the length of potential transmission seasons. Humidity changes also have the potential to change the altitudinal and latitudinal ranges of dengue vectors. In climatic models for *Ae. albopictus*, mild winters, mean annual rainfall exceeding 50cm and mean summer temperatures exceeding 20^{o}C were linked to vector establishment. While climatic factors were reported to have the potential to influence indigenous malaria transmission through accelerated parasite development and increased vector density, socio-economic developments and improvements in the availability of treatment and health care systems are expected to limit malaria re-emergence in a European context.

For sandfly-borne diseases, climate currently influences vector distribution, with sandflies largely restricted to latitudes below 45^{o}N and less than 800m above sea level, but with more recent reports of sandfly activity in Germany to 49^{o}N. Climate change is expected to make transmission of sandfly-borne diseases possible at higher latitudes, while simultaneously reducing the risk at lower latitudes due to conditions becoming too arid and hot to sustain vector survival.

In a review by Gray et al 2009, it was reported that rising temperatures directly affect the patterns of seasonal activity of ticks rather than their abundance, although this could be indirectly affected by changes in vegetation. Increases in temperature also have the potential to expand the latitude and altitude limits of disease transmission.[43] Moreover, it was suggested that increased temperatures in Central Europe may result in fewer Norway spruce and enlargement of areas colonised by Beech, which would provide a better habitat for ticks.

Climate can also affect the survival and abundance both of maintenance hosts and of pathogen-reservoir hosts. Similarly, climate can effect human activities, both short (e.g. recreational) and long-term (e.g. farming, tourism and other land use patterns) activities. All of which have the potential to affect disease incidence.

The meeting report of the ECDC expert group on climate change proposed a number of actions for Member States to enhance their preparedness for changes in disease distribution due to climate change.[44] These included:

- The implementation of exotic vector surveillance at important gates of potential species introduction (e.g. airports and harbours)
- The implementation of surveillance of and the use of clear case definitions for endemic infectious diseases
- The identification of syndromes to be monitored which would assist in monitoring (re-)emerging infectious diseases.

5. Conclusions and Recommendations

This is the first attempt in Ireland to undertake a risk assessment for the potential emergence of indigenous vectorborne disease. However, the steps taken here simply rank the risk of emergence without taking into account the public health significance of the introduction of the selected diseases. In formulating recommendations on foot of this information, other factors need to be taken into consideration, including disease severity (both for the general population and for high-risk groups).

The primary focus is on diseases ranked in likelihood rank 1 as there is evidence that disease transmission already occurs in humans in Ireland. For these, disease diagnosis, disease surveillance and prevention advice for the public are the priority activities.

For diseases in likelihood rank 2, the criteria for potential human cases appear to be met. However, a further consideration is whether the climate and other conditions in Ireland are conducive to transmission of the disease. In likelihood rank 2, consideration could be given to ensuring the availability of laboratory diagnosis and surveillance for those diseases which could result in a high burden of human illness.

For diseases at level 3, at a theoretical level at least, there are vectors in Ireland which could support the transmission of disease to humans. The threat lies in the introduction and maintenance of the pathogen in a suitable host. For the diseases ranked at likelihood rank 3 in Ireland, none assessed here have a human reservoir, with birds, rodents and other wildlife being essential for pathogen maintenance.

For diseases at level four and five, the threat level is extremely low as a result of the absence of a competent vector in Ireland. Where the vector has not been detected in Ireland, two further possibilities exist: either the climate/environment in Ireland is unsuitable to support maintenance of this vector or the vector has not yet reached Ireland but could become established as the climate is suitable.

Where climate is suitable but no vector population has been detected, monitoring for vector introduction should be considered as per ECDC/WHO advice. [57] This is particularly important for diseases where a single imported human case could serve as a pathogen reservoir, where the disease severity is high and there are implications for the blood supply.

Where no vector population has been detected and the climate in Ireland is considered unsuitable to support the maintenance of the vector, then vector surveillance should receive a very low priority.

5.1 Mosquito-borne Disease

5.1.1 Malaria

Among the mosquito-borne disease listed here, malaria was ranked as the disease with the most significant likelihood rank. Malaria is a statutorily notifiable disease in Ireland as defined by the Infectious Disease Regulations 1981 (SI No. 390 of 1981). Historically, malaria was endemic in much of Europe, with the last cases eradicated from the United Kingdom in the 1950s. It was only in 1975 that the WHO declared Europe free of malaria. The current epidemiology of malaria in Ireland is confined to imported cases, primarily associated with travel to Sub-Saharan Africa in immigrants recently settled in Ireland on visits to their country of origin to visit family. [11, 12] There are a number of *Anopheles* species present in Ireland, and thus in this risk assessment, the threat for emergence of malaria in Ireland ranked as likelihood rank 2. However, none of these species would be considered particularly efficient vectors for malaria and the current climate in Ireland would be unlikely to support local transmission, even of *P. vivax.*[45] The current prompt recognition and treatment of imported malaria cases prevents build-up of an infectious parasite reservoir, and would likely be effective at preventing indigenous transmission even if climate change were to support an increase in vector density [46].

Recommendations

- Surveillance of malaria should continue to ensure that all notified cases are travel-associated, and to inform advice for travellers in order to minimise the occurrence of imported disease
- HPSC should continue to target at risk traveller populations advising them on preventive measures such as chemoprophylaxis and mosquito bite prevention measures
- Public health professionals serving populations near to international airports should be mindful of the possibility of airport malaria

5.1.2 WNV

WNV is commonly found in Africa, West Asia, Australasia, the Middle East and in North America. There have been sporadic cases of WNV in a number of European countries in recent decades. The introduction and spread across North America since 1999 has been particularly notable.**Error! Bookmark not defined.** More recently, a large outbreak of WNV in Greece in 2010 resulted in more than 200 cases with 22 fatalities.[65] The ECDC maintains surveillance for cases of WNF throughout the year and publishes maps showing the geographical distribution of the cases on their website. The latest epidemiological information can be accessed at on the ECDC website at http://ecdc.europa.eu/en/healthtopics/west_nile_fever/West-Nile-fever-maps/Pages/index.aspx.

Cx. pipiens, a mosquito which could potentially serve as a vector for WNV is present in Ireland, raising the threat level for this disease to level 3. In other European countries where the disease has been detected from time-to-time, passive surveillance of horses and birds has proved valuable in early detection of virus introduction/ transmission. The experience of other countries such as the US and France suggests that in the event of passive surveillance for WNV in horses or birds detecting active transmission of the pathogen in an area, then testing for indigenous human WNV disease should commence.[47]

In recognition of the potential for birds and horses to serve as sentinels for detecting WNV introduction into Ireland, DAFM undertook passive surveillance of horse carcasses with neurological signs and serological surveillance of wild birds and horses.[41] No evidence of WNV was identified. Moreover, WNV infection in horses is notifiable to DAFM – [notifiable diseases of animals list is available at: http://www.agriculture.gov.ie/animalhealthwelfare/diseasecontrol/listofnotifiablediseases/].

Other factors likely to influence the potential for transmission include climate and mosquito feeding behavior.[47] WNV amplication within the vector is believed to be optimal during hot dry summers following warm winter conditions. It has been estimated that from some WNV lineages, a minimum of 109 days at 14^{o}C would be required for viral replication and dissemination to the salivary glands following uptake by the mosquito.[47] As regards feeding behaviour*, Cx. pipiens* mosquitoes in Europe appear to be largely ornithophilic (which will support the bird-mosquito-bird cycle), whereas in the US, hybrid *Cx. pipiens* which bite both humans and birds were more common.[47] These factors need to be taken into consideration alongside the rank of likelihood rank 3.

Cx. modestus is the principal WNV vector in Europe, and while it has not been reported in Ireland, there have been localized reports in the United Kingdom.[48,49] Despite this, the assessed risk of WNV in the UK remained at very low to low and the impact on the UK population was determined as low to moderate, which is in keeping with the likelihood rank 3 assessment here for Ireland.[50]

In response to the spread of *Ae. albopictus* in Europe and the recommendations of the ECDC/WHO 2007 Mission report: Chikungunya in Italy,[51] a pilot mosquito surveillance study has been initiated by the HSE-Environmental Health Service, the Zoology Dept. University College Cork and the Health Protection Surveillance Centre, to document mosquito species in Ireland. It is anticipated that this project will inform any future possible surveillance measures to monitor for the importation of exotic mosquitoes, such as *Cx. modestus*.

Recommendations

- A formal mosquito surveillance project should be established when the pilot study is complete, and serve as a trigger for further review of recommendations should evidence of *Cx. modestus* establishment be uncovered in Ireland.
- Veterinary practitioners should be encouraged to submit specimens to the DAFM laboratories from horses that display symptoms of viral encephalitis
- In the event that disease is detected in horses or wild bird populations, consideration should be given to undertaking serosurveys for evidence of human exposure among blood donors
- These recommendations should be reviewed in the event of significant climate change or the reported spread of *Cx. modestus* activity outside of current limits in Europe.

5.1.3 Chikungunya and Dengue

In southern France in 2010, La Ruche et al reported that the presence of a high density of *Ae. albopictus* vector and an increase in the number of imported dengue cases in the area facilitated local transmission of dengue for the first time in Europe since the 1920s. [52] This was followed by the occurrence of a large dengue outbreak in Madeira commencing in summer 2012. Similarly, it was a single imported case of chikungunya that is believed to have seeded a large outbreak in 2007 in the Emilia-Romagna region of Italy, an area where *Ae. Albopictus* is well-established.**Error! Bookmark not defined.** [53,]

Small numbers of imported cases of chikungunya and dengue have been reported in Ireland, any of which could serve as a source of infection for a vector. To date, none of the cases imported into Ireland have been sufficiently viraemic and have represented a very low risk of transmission. Moreover, there is no evidence of there being any suitable mosquito vectors in Ireland currently. This results in these diseases being ranked as likelihood rank 4. As dengue can cause severe disease, the prevention of establishment of *Ae. albopictus* would be of particular interest.

Monitoring for the introduction of *Ae. albopictus* was the primary objective of the pilot mosquito surveillance study referred to above. It is anticipated that this project will inform any future possible surveillance measures to monitor for the importation of exotic mosquitoes.

Recommendations

- A formal mosquito surveillance project should be established when the pilot study is complete, and serve as a trigger for further actions should a suitable vector population for dengue and chikungunya transmission be established in Ireland. The likelihood of this would increase in the event of climate change.
- Should the vectors become established in Ireland, consideration should be given to vector control measures, to surveillance for infectious agents in the established vector population, to evaluation of potential routes of virus introduction (trade in used tyres, etc), and to investigation of the likely geographical origin of the vector population through molecular technologies.
- These recommendations should be reviewed in the event of significant climate change or the reported spread of vector activity outside of current limits in Europe.

5.1.4 Other mosquito-borne diseases

Like WNV, Sindbis virus and Usutu viruses ranked at likelihood rank 3. Both these diseases currently have a very circumscribed distribution in Europe. A risk assessment for the emergence of Usutu virus in United Kingdom concluded that the public health risk was very low to low. While sufficient host and vector populations for USUV establishment were present, there was no convincing evidence of USUV in birds and no human cases had been reported in the UK. [54] Likelihood rank 3 would concur with this conclusion.

Recommendations

- No disease specific recommendations. This should be reviewed in the event of a change in the distribution of human disease in Europe.

See below for general recommendations in relation to cases of viral meningitis and viral encephalitis without microbiological confirmation

5.2 Tick-borne diseases

5.2.1 Lyme borreliosis

It has been difficult to establish the true likely burden of Lyme borreliosis in Ireland. However, Lyme borreliosis (neuroborreliosis) became a notifiable disease (S.I. No 452/2011) in 2012 so a better understanding of its epidemiology may emerge. In the first year of national surveillance, eight cases of neuroborreliosis were notified. Two cases occurred in children less than 15 years, with the remainder being adult cases. Equal numbers of male and female cases were reported. Given the small number of cases involved, a larger sample is needed before conclusions can be drawn about geographical areas at higher risk. Current understanding based on a number of published studies would suggest a high incidence in the Galway region. [22-25]

Based on this threat assessment, Lyme borreliosis ranked in likelihood rank 1. Reducing tick populations or Borrelia in wildlife reservoirs is not a practical solution in Ireland, nor elsewhere in Europe.

From a prevention perspective, the first approach by HPSC has been to provide information to the public on personal preventive measures that can be taken to reduce their risk of tick bites and on tick removal to limit the risk of disease transmission.[55] Secondary prevention relies on ensuring that clinicians are aware of the clinical features of early infection, ensuring prompt treatment and limiting the risk of more severe symptoms.[56]

Recommendations

- It is recommended that the surveillance dataset for Lyme neuroborreliosis be expanded, including the capture of risk factor information for known cases
- HPSC should continue to provide prevention advice to the public on its website www.hpsc.ie and through press releases during the peak season of cases, including information on personal preventive measures that can be taken to reduce the risk of tick bites, and on tick removal to limit the risk of disease transmission
- HPSC should develop tools to raise awareness among clinicians of the signs and symptoms of Lyme borreliosis

5.2.2 Other diseases that can be transmitted by Ixodes ricinus

While babesiosis ranked in likelihood rank 1 according to the risk assessment, this disease in humans has only been described in Ireland in asplenic patients. [15, 28, 29] The risk to the general population appears low. Moreover, the incidence of clinical babesiosis has declined in cattle although the precise reasons for this decline are unknown.[57]

Louping-ill is present in sheep in Ireland, but transmission to humans appears to be very rare and generally confined to those who have had direct contact with animal tissues rather than by vectorborne transmission. Vaccination in livestock can ensure that the risk of transmission to humans is reduced.

Tularaemia and TBE can also potentially be transmitted by *Ixodes ricinus*; however, as no human cases of either of these diseases have been reported in Ireland, they ranked as likelihood rank 3 in the risk assessment. Ecological conditions probably do not exist in Ireland for tularaemia or TBE to be become endemic.

Recommendations

- The advice to the general public for prevention of tick bites and on tick bite removal will also protect against these diseases.
- Consideration should be given to devising advice for asplenic patients in relation to babesiosis

5.2.3 Other tick-borne diseases

For the remaining tick-borne diseases assessed in this study, the ticks required for their transmission are not present in Ireland, and the conditions in Ireland are not suitable for their establishment.

Recommendations

- No further recommendations in relation to disease transmission in Ireland. This position should be reviewed in the event of significant climate change or the reported spread of vector activity outside of current limits.

5.2.4 Sandfly-borne diseases

Sandflies are not present in Ireland and the conditions here are unsuitable for their establishment. Thus all sandfly-borne diseases in this assessment ranked as likelihood rank 5. It is anticipated that in the event of climate change, there might be a gradual shift northwards in vector activity.

Recommendations

- No further recommendations are made in relation to these diseases. This position should be reviewed in the event of significant climate change or the detection of sandfly vector activity further northwards than the current limits reported.

5.2.5 A general consideration which could apply to several vectorborne diseases

For diseases such as WNF not currently endemic in Ireland, syndromic surveillance for clinical cases of viral encephalitis (VE) represents one approach to detecting emergence. Prior to 2012, only confirmed cases of VE in humans were notifiable in Ireland, limiting detection of disease emergence. In response to a study by Kelly et al 2013, a revised case definition was implemented incorporating a possible category which should promote more active monitoring of cases of VE without a microbiological diagnosis.[58]

Recommendations

- Notified clinical cases of VE should be monitored to establish if there are unexpected increases in the reported incidence, or if the epidemiology of possible VE cases differs significantly from the epidemiology of microbiologically confirmed cases.
- Consideration could be given to a national research initiative involving testing serum and CSF specimens from viral meningitis and viral encephalitis patients for emerging infections when no microbiological diagnosis is obtained following conventional testing. This could sit within a larger study involving a wider range of pathogens.

The Vectorborne Disease Sub-committee also recommends that the evidence on the threat to Ireland from vectorborne disease, and the recommendations of this report, be reviewed again in five years' time. At that time, consideration could also be given to expanding the list of diseases considered.

6. APPENDIX A

Mosquito-borne diseases

West Nile Virus Infection

WNV is a flavivirus that was first identified in the 1930s. It is commonly found in Africa, West Asia, Australasia, the Middle East and in North America. The main vectors are mosquitos of the *Culex* genus. The primary cycle involves ornithophilic mosquitos and birds. Infection can be transmitted to humans and horses. Humans and horses are considered dead end hosts. There have been sporadic cases of WNV infection in a number of European countries in recent decades. The introduction and spread across North America over the last decade was particularly notable.**Error! Bookmark not defined.**

After being bitten by an infected mosquito, about 80% of people will have no symptoms at all. Another 20% will develop a mild influenza-like illness, with fever, headache and generalised aches and pains (West Nile Fever). West Nile Fever lasts between 3 and 6 days and recovery is generally full. Fewer than 1% of infected people will go on to develop more severe disease with encephalitis and meningoencephalitis. This more severe form produces headache, high fever, stiff neck, photophobia, disorientation, muscle weakness, convulsions and coma. About 7% of those who developed neurological disease during US outbreaks died as a result of complications of infection. The risk of severe disease and death rises with increasing age. People over 50 are about 10 times more likely than children and young people to develop severe disease; the risk for those over 80 years of age is almost 50-fold higher. People with weakened immune systems may be also more vulnerable to severe disease.

West Nile Virus infection came to prominence in Europe following a large outbreak in Romania in 1996. Since then, there have been reports of human cases of WNV in a small number of European countries.[47] In 2010, WNV infection was documented for first time in humans in Greece. Between early July and August 2010, 81 cases of West Nile neuroinvasive disease were reported in the region of Central Macedonia, northern Greece.**Error! Bookmark not defined.**[5]Given that these reported cases of neuroinvasive disease represent the severe end of the disease spectrum, it is likely that the true number of cases was significantly greater. By September 2010, the total number of WNV infections had increased to 207, with 22 fatalities.[59] This outbreak in Greece is the largest outbreak of WNV in humans in Europe since the Romanian outbreak in 1996–1997.

Several other European MS reported WNV transmission in 2010. The Romanian health authorities reported a total of 18 confirmed and two probable cases of WNV infection, including two fatalities in persons over 75 years old. Moreover, three confirmed WNV cases were reported in Hungary, one confirmed case from Italy and one probable case from Portugal.[60]

The ECDC maintains surveillance for cases of WNF throughout the year, and publishes maps showing the geographical distribution of the cases on their website. The latest epidemiological information can be accessed at http://ecdc.europa.eu/en/healthtopics/west_nile_fever/West-Nile-fever-maps/Pages/index.aspx.

Chikungunya

Chikungunya fever is caused by the Chikungunya virus, an Alphavirus and member of the Togaviridae family. The primary vectors are *Aedes* mosquitoes (*Ae. aegypti, Ae. albopictus* and *Ae. polynesiensis*). Chikungunya fever is commonly found in East Africa, South and Southeast Asia. Chikungunya is not endemic in Europe. The main clinical features are fever, joint pain, muscle pain and headache. Rarely a more chronic phase can develop, with persistent joint pains. Recovery may take several weeks. Younger people tend to recover in a matter of a one or two weeks; middle-aged and elderly tend to take one to three months for full recovery. During an outbreak in La Réunion in 2006, severe complications were described, including respiratory failure, cardiovascular failure, or meningoencephalitis, with 200 deaths.

Autochthonous transmission of chikungunya fever was first reported in Europe in 2007. An outbreak in Italy primarily affected residents of (and visitors to) two villages in Emilia-Romagna, resulting in 292 suspected and confirmed human cases. The index case of the outbreak was presumed to be a resident of the region who acquired their illness in India in June 2007. Transmission within the community was possible because of the presence of a competent vector mosquito population in the area, *Ae. albopictus.*[61]

More recently, on 27 September 2010, the Institut de Veille Sanitaire in France reported the first two confirmed cases of autochthonous chikungunya on the French mainland. Both developed symptoms on 18 September 2010; neither had travelled abroad or received blood products before onset of illness.[62]

Dengue

Dengue is caused by one of four dengue virus serotypes which are flavivirus. Dengue is found commonly throughout the tropics and subtropics and is endemic in about 100 countries. The World Health Organization estimates that as many as 2.5 billion people may be at risk of Dengue and there may be as many as 50 million cases per year. Until 2010, Dengue had not been reported in Europe since the 1920's. The primary vectors are *Aedes* mosquitoes (mainly *Ae. aegypti, Ae. albopictus*). The typical illness is unpleasant with fever, chills, headache, backache and prostration (extreme exhaustion). The illness can typically last up to ten days. Full recovery is usual. In certain circumstances, the disease may progress to Dengue Haemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS), both of which can be fatal. This is rare in travellers to endemic areas, being more common in people who live in an area affected by Dengue and have been repeatedly exposed to the virus.

Two cases of autochthonous dengue fever were diagnosed in mainland France in 2010.[58] These represented the first autochthonous cases of dengue in the European Union since a large outbreak in Greece in 1927-1928.[63] The cases occurred in Nice, south-eastern France, where *Ae. albopictus* is established. Both cases recovered. La Ruche et al suggested the presence of a high density of *Ae. albopictus* vector and an increase in the number of imported dengue cases in the area in 2010 could explain this emergence. [58]

Schmidt-Chanasit et al also reported dengue fever in a German resident following travel to Croatia in 2010. [64] *Ae. albopictus* is also present in this area. In 2012, the first sustained outbreak of Dengue in the European Union since the 1920s occurred in Madeira. As of December 2012, over 2000 cases had been reported.**Error! Bookmark not defined.**,[65] *Aedes aegypti*, an effective vector for transmitting dengue

virus, had been documented on Madeira since 2005.[66] Interestingly in 2009-2010, the United States recorded the first locally acquired dengue cases in Florida since 1934.[67]

Malaria

Malaria is generally caused by one of four major species of *Plasmodium*, which are parasitic protists, although eleven species cause disease in humans. The primary vectors are *Anopheles* species; about 20/430 species are important in transmission.

Malaria is a disease of antiquity and has become a public health problem in more than 100 countries; over 2 billion people live in malarious parts of the world. More than 90% of cases occur in tropical Africa, but it is also found in southern and Southeast Asia, Central and South America, the Caribbean, the Middle East and Oceania.

Malaria produces an illness that resembles influenza with fever, chills, headache, muscle aches, and tiredness. Nausea, vomiting, and diarrhoea are not uncommon. The most severe form of malaria, that caused by *Plasmodium falciparum* may, if not promptly treated, cause kidney failure, seizures, mental confusion, coma and death. Anaemia and jaundice may occur. Haemoglobin from the burst red blood cells may be passed out in the urine, causing it to become dark in colour.

During the last 20 years, a small number of autochthonous malaria cases have occurred in EU Member States including Bulgaria, France, Germany, Greece, Italy and Spain.[45, 68] An example of this occurred in October 2010, when Spanish authorities reported their first autochthonous *P vivax* case since eradication in 1964.[69] The patient was a woman with no history of travel. The principal potential anopheline vector of malaria in Spain is *An. atroparvus* which can transmit *P. vivax.*

Generally, these cases are sporadic but in Southern Greece in 2009, a small outbreak was reported. Eight hospitalized cases of locally acquired *P. vivax* malaria occurred.[68] An Albanian malaria case was also reported to have likely acquired their illness in the same region of Greece at this time. According to VBORNET (the European Network for Arthropod Vector Surveillance for Human Public Health), several Anopheline vector species which are competent for *P. vivax* are known to breed in Greece, including *An. atroparvus*, *An. sacharovi* and *An. superpictus.*[68] In 2011, further autochthonous cases of *P. vivax* were reported in Greece.**Error! Bookmark not defined.** According to Danis et al fifteen Anopheles species occur in Greece, of which five are considered as potential malaria vectors, namely *An. claviger, An. hyrcanus, An. maculipennis, An. sacharovi* and *An. superpictus.***Error! Bookmark not defined.**

Sindbis virus

Sindbis virus is an alphavirus which is associated with fever, rash and arthritis. It is a mosquito-borne disease found in Africa, Australia and Europe, the main vectors being ornithophilic *Culex*, *Culiseta* and to a lesser extent *Aedes* mosquitos. Redwings, fieldfares, chaffinches, blue tits and song thrushes are believed to be amplifying hosts. Transmission to humans is mainly by *Aedes cinereus* Meigen.[70] In Finland, Sindbis virus causes Pagosta disease, and has been responsible for outbreaks of human disease there about every seven years since the early 1970s. It has been suggested the successive rises and crashes in grouse population may be linked to this cycle. Similar clinical illness has been reported from Sweden (Ockelbo disease).

Usutu virus (USUV)

Usutu virus is a mosquito-borne Flavivirus. It appeared in Europe for the first time in Austria in 2001, causing significant mortality in several species of wild birds, including blackbirds. Emerging herd immunity over subsequent years resulted in a decline in bird mortality over the next few years. The virus was subsequently detected in dead birds in Hungary, Switzerland and Italy. *Culex* species are a likely vector, and Usutu virus has been detected in overwintering *Cx. pipiens* mosquitos. The virus appears to be able to infect humans without generally inducing severe disease; in particular, it may be associated with a transient rash.[71] In 2009, Pecorari et al reported on the first human case of neuroinvasive Usutu virus infection in Italy.[72] The patient was likely to be immunosuppressed due to underlying disease and its treatment.

Tick-borne diseases

Lyme borreliosis

Lyme borreliosis is the most prevalent tick-borne zoonosis in the northern hemisphere, and is considered an emerging disease in Europe.[73] It is caused by *Borrelia burgdorferi* sensu lato (LB borrelia), different species of which cause varying symptoms in humans, and not all of which are pathogenic. An early symptom of human infection is erythema migrans, a migrating reddish rash that occurs in a large proportion of infections. There may be more serious symptoms involving the nervous system, joints, the heart or other tissues. While clinical disease can be severe, it is rarely fatal.

The species most commonly associated with disease in humans are *B. afzelii*, *B. burgdorferi* sensu stricto and *B. garinii*, the role of other species being less certain. The disease is transmitted to humans by hard-bodied ticks: in Europe the sheep tick *Ixodes ricinus* and the taiga tick *I. persulcatus* are considered the primary vectors to humans, but other ticks may play a role in the enzootic cycle, but are rarely involved in clinical transmission.

Disease risk is determined by tick prevalence, *Borrelia* infection rates in ticks, and human interaction with tick habitats. *I. ricinus* has a three stage life cycle: larva, nymph and adult with the entire life cycle usually taking from 2-4 years, but may last up to seven. All stages depend on blood meals to enter the next stage and attach themselves to hosts using specialised mouthparts and salivary secretions. All the large animals, especially deer, can feed large numbers of immature ticks as well as adults. Small rodents tend to feed more larvae than nymphs while large to medium sized animals tend to feed a greater

proportion of the nymphal than larval population. Adults only feed on large and medium sized animals. There is variation in the peak season in questing behaviour from the three stages, with larvae peaking between May and September and nymphs between February and November.

Borrelia colonise the mid gut of infected ticks and migrate to the salivary glands after the tick attaches to the new host. The time needed for this transfer varies by *Borrelia* species, but it is generally advised that removal of ticks within 24 hours reduces the risk of disease transmission.

Tick-borne encephalitis (TBE)

Tick-borne encephalitis (TBE) is a viral infectious disease that attacks the central nervous system and can result in long-term neurological symptoms and even death. Approximately two-thirds of human TBE virus infections are asymptomatic. In clinical cases, TBE often has a biphasic course. The first viraemic phase is associated with non-specific symptoms (fever, fatigue, headache, myalgia, nausea). This phase is followed by an asymptomatic interval that precedes the second phase, when the central nervous system is involved (meningitis, meningoencephalitis, myelitis, paralysis, radiculitis). [74]

The disease is found in many parts of Europe and Asia. It is caused by a virus (Flavivirus genus, family Flaviviridae) which includes three subtypes, the European subtype, the Siberian subtype and the far eastern subtype. The European subtype is endemic in rural and forested areas of central, eastern and northern Europe, while the Siberian subtype has been associated with some areas in north-eastern Europe. Both these subtypes have case fatality rates of up to 3%, considerably lower than the 35% case fatality rates reported for the far eastern subtype. The far eastern subtype is most commonly associated with China, Japan and Eastern Russia.

The virus is transmitted to humans by the bite of infected ticks, found in woodland habitats. *Ixodes ricinus* ticks is the vector for the European subtype and *I. persulcatus* is the vector for the Siberian subtype. Reservoir hosts for the TBE virus are mainly small rodents (voles, mice), while a variety of other hosts (e.g., foxes, bats, hares, deer, wild boar, sheep, cattle, goats, dogs) support the tick life cycle, thus indirectly supporting virus multiplication. Co-feeding (transfer of virus from nymphs to larvae without a viraemia) mean that many of these animals might contribute to transmission. Co-feeding transmission is thought to be the main means of transmission, even in rodents which have very transitory viraemias. Humans are incidental and dead-end hosts.

The disease may also be transmitted through consumption of infected unpasteurised dairy products. Tick-borne encephalitis virus is not directly transmitted from human to human, apart from the possibility of vertical transmission from an infected mother to the foetus.

Louping-ill

Louping-ill is caused by louping-ill virus (LIV), a flavivirus, which is closely related to the TBE virus. It is an infection of the central nervous system and is acquired from the bite of an infected tick (*Ixodes ricinus*). It primarily affects sheep but can infect cattle, horses, pigs, dogs, deer and other wildlife species. It is an important disease of grouse. Clinical cases are occasionally reported in sheep in Ireland.[30] Louping-ill only occasionally causes human disease.[75]

Human cases are very uncommon, and most of the recorded cases have occurred in laboratory or abattoir workers. Direct contact with infected animal tissues has been reported as method of transmission, particularly if these are handled in a manner which generates aerosols.

Congo Crimean Haemorrhagic Fever (CCHF)

The CCHF virus is a member of the genus *Nairovirus* of the *Bunyaviridae* family. It causes an illness in humans which presents as high fever of sudden onset, malaise, severe headache and gastrointestinal symptoms. Haemorrhagic symptoms sometimes occur in late stages of the disease.[76] High case fatality rates (10-50%) have been reported and the disease is considered difficult to treat. It is endemic in parts of Africa, Asia and the Middle East. In Europe cases of human infections have been reported from Albania, Armenia, Bulgaria (where it has been endemic since the 1950s), Kazakhstan, Kosovo, Russia, Serbia, Tajikistan, Turkey, Turkmenistan, Ukraine and Uzbekistan. In June 2008, Greece reported its first case.**Error! Bookmark not defined.**

CCHF is transmitted to humans mainly by *Hyalomma* ticks and the main zoonotic reservoirs include domestic animals such as cattle, sheep, goats and hares. *Hyalomma* ticks are two-host ticks. Larvae and nymphs also feed on hedgehogs and birds, rodents are rarely involved. Humans are not the preferred hosts of *Hyalomma* ticks and are infrequently bitten compared to livestock. When infected, ticks can transmit CCHF virus throughout their life and the infection is also transmitted to the next generation of tick transovarially. *H. marginatum*, the main vector in Europe, is distributed across south-eastern and southern Europe. It was most recently detected for the first time in the Netherlands and southern Germany in 2006. It has been predicted that the distribution of *Hyalomma* ticks will change in response to climate change, leading to an extension of the range for CCHF, in particulate to other Mediterranean countries.**Error! Bookmark not defined.**

Transmission to humans is also possible by direct contact with the blood or tissues of viraemic hosts. Nosocomial transmission may occur through direct contact with infected blood or body fluids or through contaminated medical equipment or supply

Tularaemia

Tularaemia is a zoonosis caused by the bacterium *Francisella tularensis,* which is transmitted by ticks, mosquitos, flies and through direct animal contact[77]. Rabbits, hares, squirrels, foxes and ticks can all serve as reservoirs.

High fever is a feature of infection, but other symptoms varying with the portal of entry. Symptoms may include swollen lymph glands, eye infection, throat infection, pneumonia and severe infection with blood stream infection. There are currently four subspecies known: *tularensis* (the most virulent, previously called type A), *holarctica* (the most widespread, formerly called type B), *mediasiatica,* and *novicida* (the least virulent). *F. tularensis* is distributed across the Northern Hemisphere, but subspecies *tularensis* only occurs in North America and *mediasiatica* in central Asia. In Europe, the countries with the highest incidence rates include Finland, Sweden, Hungary, Slovak Republic, Serbia, Montenegro, Czech Republic and Bulgaria.[77]

Dermacentor reticulatus, D. marginatus, *Ixodes ricinus*, and *Haemaphysalis concinna* ticks are believed to be the principal vectors in Europe. Tabanids (especially deer flies) are likely to be more significant than mosquitoes in mechanical transmission of tularaemia.

Babesiosis

Human transmission of *Babesia* species in Europe is mainly due to *Ixodes ricinus,* the ubiquity of this tick creates a risk across Europe. The small number of known human cases in Europe have been clinically severe and were attributed to *B. divergens*, *B. venatorum* (EU1) and *B. microti*. Bovine *B. divergens* babesiosis is widely distributed on the European continent.

Human babesiosis also occurs in the USA, Africa, Mexico, Japan, Taiwan and India. Most infections however, seem to remain asymptomatic. The incubation period varies between one and eight weeks, but can be several months. The intensity of clinical signs of babesiosis in humans varies from mild to severe, ranging from non-specific flu-like symptoms, to shock-like syndrome with renal failure and pulmonary oedema, which may be fatal.

Cattle, roe deer and rodents are reservoirs of *B. divergens*, *B. venatorum* and *B. microti* respectively. Note that, unlike in the USA, only one *B. microti* case has been authenticated in Europe despite the widespread occurrence of the parasite in rodents. The *Ixodes ricinus* tick is also the reservoir of *B. divergens* and *B. venatorum* because of the transovarial and transstadial transmission of the protozoa in the tick host. In Europe, human transmission occurs mainly by an *Ixodes ricinus* tick bite. Elsewhere, human infection by blood transfusion has also been documented, with transplacental and perinatal transmission described more rarely.

Clinical babesiosis, manifesting as haemoglobinuria ('redwater'), was once commonplace in Irish cattle. *B. divergens* was transmitted by *I ricinus* and usually occurred after naïve cattle were moved from disease free to disease endemic areas of permanent pasture. The incidence appears to have reduced significantly in cattle over recent decades but the reasons for this reduction in incidence are not known with any certainty.

Human cases occur mostly in splenectomised or immunocompromised patients and exposure to ticks represents the main risk factor for infection. Prevention is limited to avoiding tick bites and promoting personal measures of protection against ticks, with particular attention to splenectomised and immunologically compromised patients. The possible risk of infection through blood transfusion needs to be controlled in particular for splenectomised or immunologically compromised patients.[78]

Infections transmitted by sandflies

Viruses transmitted by sandflies

Although sandflies are also implicated in the transmission of Vesiculovirus and Orbivirus, it is transmission of Phlebovirus, which includes sandfly fever Sicilian virus, sandfly fever Naples virus, and Toscana virus, that are most significant in European terms. All three are endemic in the Mediterranean region.[79]

Sandfly fever Sicilian virus

With sandfly fever Sicilian virus, patients present with influenza-like symptoms including fever, retro-orbital pain, myalgia and malaise and usually recover fully within a week. The estimated distribution limits for human disease include Serbia, southern Italy, Greece and Cyprus. A number of different vector species have been proposed as the primary vector for sandfly fever Sicilian virus including *P. papatasi* for Cyprus, *Phlebotomus* belonging to the subgenus *Larroussius* (*P. perniciosus, P. perfiliewi* and *P. neglectus*) for Italy and *P.* (*Larroussius*) *neglectus* for a closely related virus called Corfou virus in Greece. Rodents may be involved in maintenance of the life cycle.[79]

Sandfly fever Naples virus

For Naples virus, the disease course is similar to sandfly fever Sicilian virus. Serbia has been the most consistent focus of infection, with the estimated distribution limit including southern Italy. The virus has been isolated from *P. perniciosus* (Italy), *P. perfiliewi* (Serbia) and *P. papatasi* (Egypt). Reservoirs for Sandfly fever Naples virus are unknown.[79]

Toscana virus

In contrast, many infections with the Toscana virus are asymptomatic, but outbreaks of acute meningitis or meningo-encephalitis due to infection with Toscana virus have been reported in Mediterranean countries (Italy, France, Spain and Portugal). In summertime in Italy, Toscana virus is responsible for 80% of meningitis and meningo-encephalitis cases in children and 50% of meningitis and meningo-encephalitis cases in adults. Potential vectors include *P. perniciosus* and *P. perfiliewi* belonging to the subgenus *Larroussius*. It is suggested that the reservoir of Toscana virus is most likely the vector itself, although it is unlikely to be maintained indefinitely by vertical transmission. There is also the possibility of unknown reservoirs.[79]

Leishmaniasis

Leishmaniasis is caused by parasitic protozoa of the genus *Leishmania*. Humans are infected via the bite of phlebotomine sandflies, which breed in forest areas, caves or the burrows of small rodents.[80] There are four main types of the disease:

- In cutaneous forms, skin ulcers usually form on exposed areas, such as the face, arms and legs. These usually heal within a few months, leaving scars.
- Diffuse cutaneous leishmaniasis produces disseminated and chronic skin lesions resembling those of lepromatous leprosy. It is difficult to treat.
- In mucocutaneous forms, the lesions can partially or totally destroy the mucous membranes of the nose, mouth and throat cavities and surrounding tissues.
- Visceral leishmaniasis, also known as kala azar, is characterized by high fever, substantial weight loss, swelling of the spleen and liver and anaemia. If left untreated, the disease can have a fatality rate as high as 100% within two years.

Two parasites are currently endemic in Europe: *Leishmania infantum* which causes zoonotic visceral and cutaneous leishmaniasis in humans and dogs (the reservoir host) and *L. tropica* which causes anthroponotic cutaneous leishmaniasis.[81]

Disease due to *L. infantum* occurs throughout the Mediterranean region, while that caused by *L. tropica* occurs sporadically in Greece. These two transmission cycles are both widespread in the neighbouring Middle East and in North Africa. Visceral leishmaniasis due to the members of the *L donovani* complex other than *L tropica* has been reported in Cyprus.

Fewer than 50 of the approximately 1,000 species of sandflies are vectors of leishmaniasis worldwide. Vector competence is influenced by their ability to support the development of infective stages in their gut and the potential for ecological contact with reservoir hosts.

It has been reported that the principal vectors of *L. infantum* in the Mediterranean region are members of the subgenus *Larroussius* (includes *Phlebotomus ariasi*, *P. perniciosus* and *P. perfiliew*) and that *P. sergenti sensu lato* is likely to be the main vector of *L. tropica.*

New evidence in recent years has indicated that transmission of *L. infantum* may also be possible through needle transmission (IDUs), vertical transmission in dogs, horizontal transmission in dogs by biting, and even vertical transmission in humans from mother to child.

Glossary

Autochthonous -originating in the place where found, is native to an area

CSO - Central Statistics Office

DAFM – Department of Agriculture, Food and the Marine

DEFRA – United Kingdom Department of Food and Rural Affairs

ECDC – European Centre for Disease Prevention and Control

PHE – Public Health England

HPSC – Health Protection Surveillance Centre

HSE – Health Service Executive

MS – Member States of the European Union

NVRL – National Virus Reference Laboratory

Ornithophilic – preference for feeding on avian species

WHO - World Health Organization

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